Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1. (Currently amended) A method of delivering a medicant to an abnormal brain region in a mammalian subject, comprising: administering to a mammalian subject having an abnormal brain region an agonist of a calcium-activated ~~or ATP-sensitive~~ potassium channel, the agonist being other than bradykinin or a bradykinin analog, under conditions and in an amount sufficient to selectively increase the permeability to the medicant of a capillary or arteriole delivering blood to cells of the abnormal brain region; and administering to the subject simultaneously or substantially simultaneously with the agonist the medicant, so that the medicant is delivered selectively to the cells of the abnormal brain region compared to normal brain regions.

Claims 2-109. (Cancelled)

Claim 110. (New) The method of Claim 1, wherein the abnormal brain region is a region of brain tissue physiologically affected by injury, trauma, infection, stroke, or ischemia.

Claim 111. (New) The method of Claim 1, wherein the abnormal brain region is a region of brain tissiue physiologically affected by stroke.

Claim 112. (New) The method of Claim 1, wherein the abnormal brain region is region of tumor tissue.

Claim 113. (New) The method of Claim 1, wherein the abnormal brain region is a region of benign tumor tissue.

Claim 114. (New) The method of Claim 1, wherein the abnormal brain region is a region of malignant tumor tissue.

Claim 115. (New) The method of Claim 1, wherein the abnormal brain region includes a glioma, glioblastoma, oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodermal tumor, atypical meningioma, malignant meningioma, neuroblastoma, sarcoma, melanoma, lymphoma, or carcinoma.

Claim 116. (New) The method of Claim 1, wherein the agonist is NS1619.

Claim 117. (New) The method of Claim 1, wherein the agonist is 1-EBIO.

Claim 118. (New) The method of Claim 1, wherein the agonist is a guanylyl cyclase activator.

Claim 119. (New) The method of Claim 118, wherein the guanylyl cyclase activator is a metalloporphyrin.

Claim 120. (New) The method of Claim 119., wherein the metalloporphyrin is a zinc protoporphyrin or a tin protoporphyrin IX.

Claim 121. (New) The method of Claim 118, wherein the agonist is a guanylyl cyclase activating protein.

Claim 122. (New) The method of Claim 1, wherein the mammal is a human.

Claim 123. (New) The method of Claim 1, wherein the medicant is a therapeutic cytotoxic agent.

Claim 124. (New) The method of Claim 1, wherein the medicant is cisplatin.

Claim 125. (New) The method of Claim 1, wherein the medicant is carboplatin.

Claim 126. (New) The method of Claim 1, wherein the medicant is methotrexate.

Claim 127. (New) The method of Claim 1, wherein the medicant is 5-fluororacil.

Claim 128. (New) The method of Claim 1, wherein the medicant is amphotericin.

Claim 129. (New) The method of Claim 1, wherein the medicant is daunorubicin.

Claim 130. (New) The method of Claim 1, wherein the medicant is doxorubicin.

Claim 131. (New) The method of Claim 1, wherein the medicant is vincristine.

Claim 132. (New) The method of Claim 1, wherein the medicant is vinblastine.

Claim 133. (New) The method of Claim 1, wherein the medicant is busulfan.

Claim 134. (New) The method of Claim 1, wherein the medicant is chlorambucil.

Claim 135. (New) The method of Claim 1, wherein the medicant is cyclophosphamide.

Claim 136. (New) The method of Claim 1, wherein the medicant is melphalan.

Claim 137. (New) The method of Claim 1, wherein the medicant is ethyl ethanesulfonic acid.

Claim 138. (New) The method of Claim 1, wherein the medicant is a protein.

Claim 139. (New) The method of Claim 1, wherein the medicant is an antimicrobial agent or antibiotic.

Claim 140. (New) The method of Claim 1, wherein the medicant is a monoclonal antibody or antigen-binding antibody fragment.

Claim 141. (New) The method of Claim 1, wherein the medicant is a cytokine, cytokine agonist or cytokine antagonist.

Claim 142. (New) The method of Claim 141, wherein the cytokine is an interferon.

Claim 143. (New) The method of Claim 141, wherein the cytokine is a transforming growth factor.

Claim 144. (New) The method of Claim 143, wherein the transforming growth factor is transforming growth factor-β.

Claim 145. (New) The method of Claim 141, wherein the cytokine is tumor necrosis factor- α.

Claim 146. (New) The method of Claim 141, wherein the cytokine is a interleukin.

Claim 147. (New) The method of Claim 1, wherein the cytokine is interleukin-2.

Claim 148. (New) The method of Claim 1, wherein the medicant is an immunotoxin and immunosuppressive.

Claim 149. (New) The method of Claim 1, wherein the medicant is a boron compound.

Claim 150. (New) The method of Claim 1, wherein the medicant is an adrenergic agent.

Claim 151. (New) The method of Claim 1, wherein the medicant is an anticonvulsant.

Claim 152. (New) The method of Claim 1, wherein the medicant is an ischemia-protective agent.

Claim 153. (New) The method of Claim 152, wherein the medicant is a a N-methyl-D-aspartate (NMDA).

Claim 154. (New) The method of Claim 1, wherein the medicant is an antitrauma agent.

Claim 155. (New) The method of Claim 1, wherein the medicant is a diagnostic agent.

Claim 156. (New) The method of Claim 1, wherein administering the agonist is by intravenous or intra-arterial infusion or injection.

Claim 157. (New) The method of Claim 1, wherein administering the agonist is by intracarotid infusion or injection.

Claim 158. (New) The method of Claim 1, wherein the agonist is administered to the mammalian subject by a bolus injection.

Claim 159. (New) The method of Claim 1, wherein the agonist is administered to the mammalian subject in an amount from about 0.075 to 1500 micrograms per kilogram body mass.

Claim 160. (New) The method of Claim 159, wherein the agonist is administered to the subject in an amount from about 0.075 to 150 micrograms per kilogram body mass.

Claim 161. (New) The method of Claim 159, wherein the agonist is administered to the mammalian subject at a dose rate of about 0.075 to about 100 $\mu g\ kg^{-1}\ min^{-1}$ for up to about 30 minutes.

Claim 162. (New) The method of Claim 159, wherein the agonist is administered to the mammalian subject at a dose rate of about 0.075 to about 15 $\mu g\ kg^{-1}\ min^{-1}$.

Claim 163. (New) The method of Claim 1, wherein the medicant is administered via intravenous, intramuscular, intra-arterial, or intracarotid injection or infusion.

Claim 164. (New) The method of Claim 1, wherein the agonist and the medicant are administered via intracarotid infusion or injection.

Claim 165. (New) A method of selectively delivering a medicant to an abnormal brain region in a mammalian subject, comprising: administering to a mammalian subject having an abnormal brain region an agonist of a calcium-activated potassium channel, the agonist being other than bradykinin or a bradykinin analog,-under conditions and in an amount sufficient to increase potassium flux through a calcium-activated potassium channel in an endothelial cell membrane of a capillary or arteriole delivering blood to cells of the abnormal brain region, whereby the capillary or arteriole is made more permeable to the medicant; and administering to the subject simultaneously or substantially simultaneously with the agonist the medicant, so that the medicant is delivered selectively to the cells of the abnormal brain region compared to normal brain regions.

Claim 168. (New) A pharmaceutical composition comprising a combination of an agonist of a calcium-activated potassium channel, the agonist being other than bradykinin or a bradykinin analog, formulated in a pharmaceutically acceptable solution together with a therapeutic cytotoxic agent for delivery by intravascular infusion or injection into a mammal.

Claim 169. (New) The pharmaceutical composition of Claim 168, wherein the agonist is present in an amount of about 0.075 to 1500 micrograms per kilogram body mass .

Claim 170. (New) The pharmaceutical composition of Claim 168 wherein the agonist is present in an amount of about 0.075 to 150 micrograms per kilogram body mass.

Claim 171. (New) The pharmaceutical composition of Claim 168, wherein the agonist is NS1619.

Claim 172. (New) The pharmaceutical composition of Claim 168, wherein the agonist is 1-EBIO.

Claim 173. (New) The pharmaceutical composition of Claim 168, wherein the agonist is a guanylyl cyclase activator.

Claim 174. (New) The pharmaceutical composition of Claim 173, wherein the guanylyl cyclase activator is a metalloporphyrin.

Claim 175. (New) The pharmaceutical composition of Claim 174, wherein the metalloporphyrin is a zinc protoporphyrin or a tin protoporphyrin IX.

Claim 176. (New) The pharmaceutical composition of Claim 168, wherein the agonist is a guanylyl cyclase activating protein.

Claim 177. (New) The pharmaceutical composition of Claim 168, wherein the therapeutic cytotoxic agent is cisplatin.

Claim 178. (New) The pharmaceutical composition of Claim 168, wherein the therapeutic cytotoxic agent is carboplatin.

Claim 179. (New) The pharmaceutical composition of Claim 168, wherein the therapeutic cytotoxic agent is methotrexate.

Claim 180. (New) The pharmaceutical composition of Claim 168, wherein the therapeutic cytotoxic agent is 5-fluororacil.

Claim 181. (New) The pharmaceutical composition of Claim 168, wherein the therapeutic cytotoxic agent is amphotericin.

Claim 182. (New) The method of Claim 168, wherein the therapeutic cytotoxic agent is daunorubicin, doxorubicin, vincristine, or vinblastine.

Claim 183. (New) The pharmaceutical composition of Claim 168, wherein the therapeutic cytotoxic agent is busulfan, chlorambucil, cyclophosphamide, melphalan, or ethyl ethanesulfonic acid.

Claim 184. (New) A pharmaceutical composition comprising a combination of an agonist of a calcium-activated potassium channel formulated together in a pharmaceutically acceptable solution together with a drug for delivery by intravascular infusion or injection, wherein the drug is a protein, antimicrobial agent, antibiotic, interferon, cytokine, cytokine agonist, cytokine antagonist, monoclonal antibody, antigen-binidng antibody fragment, immunotoxin, immunosuppressant, ischemia-protective agent, adrenergic agent, boron compound, anti-convulsant, anti-trauma agent or diagnostic agent.

Claim 185. (New) The pharmaceutical composition of Claim 184, wherein the drug is a protein.

Claim 186. (New) The pharmaceutical composition of Claim 184, wherein the drug is a an antimicrobial agent or antibiotic.

Claim 187. (New) The pharmaceutical composition of Claim 184, wherein the drug is cytokine, cytokine agonist or cytokine antagonist.

Claim 188. (New) The pharmaceutical composition Claim 184, wherein the cytokine is an interferon.

Claim 189. (New) The pharmaceutical composition of Claim 187, wherein the cytokine is a transforming growth factor.

Claim 190. (New) The pharmaceutical composition of Claim 187, wherein the cytokine is tumor necrosis factor- α.

Claim 191. (New) The pharmaceutical composition of Claim 187, wherein the cytokine is a interleukin.

Claim 192. (New) The pharmaceutical composition of Claim 184, wherein the drug is an immunotoxin or immunosuppressant.

Claim 193. (New) The pharmaceutical composition of Claim 184, wherein the drug is a boron compound.

Claim 194. (New) The pharmaceutical composition of Claim 184, wherein the drug is an adrenergic agent.

Claim 195. (New) The pharmaceutical composition of Claim 184, wherein the drug is an anticonvulsant.

Claim 196. (New) The pharmaceutical composition of Claim 184, wherein the drug is an ischemia-protective agent.

Claim 197. (New) The pharmaceutical composition of Claim 196, wherein the drug is a N-methyl-D-aspartate (NMDA).

Claim 198. (New) The pharmaceutical composition of Claim 184, wherein the drug is an antitrauma agent.

Claim 199. (New) The pharmaceutical composition of Claim 184, wherein the drug is a diagnostic agent.

Claim 200. (New) A kit for enhancing the delivery of a medicant to an abnormal brain region, comprising: an agonist of a calcium-activated potassium channel, said agonist being other than bradykinin or a bradykinin analog; and instructions for using the agonist for enhancing the delivery of a medicant to an abnormal brain region by increasing the permeability of a capillary or arteriole delivering blood to cells of the abnormal brain region.

Claim 201. (New) The kit of Claim 200, wherein the agonist is NS-1619.

Claim 202. (New) The kit of Claim 200, wherein the agonist is 1-EBIO.

Claim 203. (New) The kit of Claim 200, wherein the agonist is a guanylyl cyclase activator.